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INFLUENZA AND THE NERVOUS SYSTEM.

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REPRINTED FROM
THE PHILADELPHIA MEDICAL JOURNAL.
1902.

Reprinted from THE PHILADELPHIA MEDICAL JOURNAL, Dec. 27, 1902

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In this day and generation, when statistical tables are voluminous and illy digested, it is a comparatively simple matter to make a brief for almost any relationship of cause and effect, even for unrelated phenomena. Many and widely distributed have been the topics which have needed the support of the statistical argument, but the relationship of influenza to the nervous system does not rest on such a substratum. The value of statistics, however, is helpful in bringing to the fore some of the more important features of the toxemia of influenza.

Of the history of influenza epidemics it is but necessary to mention that, according to Fehr[1], von Koenigshoven described a markedly virulent epidemic, which occurred in 1387, which was universal over the entire European area; de Bays described an epidemic, occurring in 1404, and Fehr mentions the interesting fact that it was then noted that following the disease there was a tendency to mental trouble: Hypochondriasis, melancholia, depression and even suicide.

The last epidemic began in 1889 and 1890, after a period of forty years of comparative immunity. It had been the experience in former epidemics, in so far as medical literature affords us an insight into their history, that the disease raged for two or

*Read before the Section of Hygiene and Public Health, American Medical Association, 1902.

three years, abated and finally disappeared; but the history of the present invasion has been far from this. Influenza has been epidemic almost every year since 1890, in this country at least, and, if we can judge from the English writers[2], the same conditions have prevailed in Great Britain. An editorial writer there says: "This is the tenth consecutive winter during which epidemic influenza has prevailed in Great Britain. The epidemic began, it will be remembered, in October, 1889, after a period of immunity which had lasted for nearly forty years. It was hoped at the time that, after prevailing for one, two or, at most, three years, the epidemic would pass away, as had been observed on previous occasions, but this anticipation has been, to a great extent, falsified, and the annual recurrences, although they have not been so extensive as during the first two years, have been sufficiently widespread to cause very serious inconveniences on many occasions, very distinct increase in the death-rate, and, as is generally believed, a notable accession to the number of chronic maladies, especially of the nervous system, which are characteristic of the present generation."

Numerous other reports confirm the opinion that this influenza epidemic has been remarkable for its universality. Norway and Sweden, Italy, Turkey[3], Russia and Greece, all have shown a marked epidemicity. Whereas this chronicity has been unparalleled, yet, at the same time, in so far as the United States is concerned, there seems to have been a distinct period of comparative quiescence with, in 1900-1901, a recrudescence. With this recrudescence, if the influences of suggestion can be eliminated, it would seem that the disease was of a different type, or rather that one particular portion of the body bore the brunt of the attack, namely, the nervous system. This point of view was stated in the *Medical News*[4], in the letter from the London correspondent of that publication, who wrote: "And still the influenza spreads in London, in spite of beautifully

mild, bright, sunny weather for two weeks past. All practitioners report the type of the disease as quite mild, and yet the death-rate keeps steadily rising from 22, four weeks ago, to 50, 74 and, last week, 113 deaths per week. One cannot help suspecting that, as in previous epidemics, influenza, like charity, covereth a multitude of sins of careless diagnosis, and that, even when it is the precipitating cause of death, it acts simply by striking some previously weak point in the defences of the organism, or lighting up some smouldering internal mine, like tuberculosis, fatty heart or granular kidney. No disease in the realm of nosology threatens so much and does so little, or produces so large a percentage of vivid fear of dissolution, with so low a death-rate.

"For the most part, in this epidemic affections of the nervous system seem to predominate, and many cases are scarcely recognizable until the characteristic stage of depression sets in, and, fortunately, as might have been expected from the general absence of catarrhal symptoms, few secondary infections with pneumonic and bronchitic inflammations are reported. In fact, curiously enough, the total death-rate is still below the mean average for these weeks of the year, and no marked increase in the mortality from respiratory diseases has yet occurred."

The question is pertinent as to the interpretation of the foregoing. May it not be true that the action of the Canon-Pfeiffer bacillus is being seen more and more in its true colors and that, like the bacillus of diphtheria, it has a specific action on the nervous system, and that this is being recognized more clearly than ever before?

It has already been pointed out that, as early as the fourteenth century, its influence of causing psychoses was recognized, and the more recent words of Kellogg, Gowers and Berkeley only serve to accentuate a belief now grown almost universal.

Thus, Kellogg[5] says: "Epidemic influenza (grippe) gives rise to some very serious forms of insanity, lingering and uncertain as to recovery, and this is particularly the case in elderly persons." It is to be regretted that this excellent clinical observer does not go more into detail on this question.

Gowers[6] writes: "There is no acute malady, with the exception of diphtheria, after which disturbance of the nervous system is so frequent as after influenza, and there is certainly no disease that has such varied nervous sequelæ. This effect, though long known, has never been perceived so distinctly as in the severe outbreak of 1890.

"Functional disturbances of the nervous system seem to be the direct effect of the action of the toxins of the bacillus, since they form almost constant features of the acute affection. Some of the more severe sequelæ, moreover, have followed second or third attacks of influenza, which were mild and sometimes even trifling. On the other hand, there has been a disposition to associate with influenza affections of the nervous system coming on six, nine or twelve months after the primary disease, without any other connection with this than some impairment of constitutional strength, such as follows every depressing acute illness. Such remote affections cannot be regarded as the specific consequences of influenza. Moreover, many of the direct sequelæ cannot be regarded as quite special, since so often previous disposition to them can be distinctly traced.

"The mental state and physical depression or inertia, seldom absent, rarely cease with the acute attack; this almost universal sequel has become familiar to every one. It is not surprising that, especially in predisposed individuals, definite melancholia should grow out of it, sometimes of the hypochondriacal type, sometimes with definite delusions, and occasionally with suicidal impulses."

More recently, Berkeley[7] states: "Following the

epidemic of la grippe in 1891-1892, and the more recent one of 1898-1899, a variety of nervous disturbances was quite prevalent, mainly in persons of latent or pronounced psychopathic disposition. The majority of the forms assumed have been those of a general neurasthenia of a severer or milder type, but there has also been quite an array of the true psychoses. The toxins of influenza seem to fall with especial stress upon the central nervous system and, besides, have a most definite depleting effect upon the general physical powers, both of which influences act with greater force upon the hereditarily unstable than upon the sound individual. At the autopsies of patients dying from the influenza poison the central nervous system is always found much congested (Geill).

"The most frequent form of psychoses following influenza is the acute confusion, at a later stage assuming the clinical picture of a hallucinatory, agitated melancholia. Mixed hypochondriacal and neurasthenic forms are also noted. The duration is comparatively short, from two to six weeks, and the eventual outcome is favorable, unless the predisposition to insanity is great.

"Stuporous states occur with less frequency than the above form, but are of longer duration, running their course, as a rule, in from eight to ten weeks. All the instances under my personal observation have been fully restored to sanity. The majority of cases is found between the twentieth and fiftieth years, very few in childhood or old age."

With this statement my experience coincides. In an analysis of some fifty patients seen in the last five years suffering from influenzal psychoses, mental stupor or confusion has been a prominent symptom in over 20%. The affinities with neurasthenia are evident.

Wildermuth[8], in his work, also observes that the great epidemic of 1898-1899 was followed by a long-

continued state of nervous depression in many persons in Germany. For prognosis he observes that of 52 personal patients there were 26 recoveries, 17 remained insane and 9 died.

It is a point of no little importance, before going further with this inquiry, to insist that there is a marked difference between what is known as a cold and real influenza. It cannot be gainsaid that the symptoms in either case may be practically identical, but it seems evident, from the investigations of Canon, Pfeiffer, Wynekoop and others, that in nearly all cases a diagnosis may be made by means of the microscope, and that this procedure is imperative.

Concerning the Bacteriology of Influenza.

In an editorial, contributed to the January 14 (1899) issue of the *Journal of the American Medical Association*, on the recent recrudescence of influenza, it was suggested[9] that it would be more profitable than any special observations of the geographical and historical pathology of the disease, as proposed by the Marine-Hospital Bureau, "to take advantage of the present outbreak to study the bacteriology of influenza with reference to certain mooted points of the greatest interest—to physicians, as to treatment—and to sanitarians, as to prevention.

"Is there," is asked, "an influenza vera due to a special germ, the Canon-Pfeiffer, the toxin of which profoundly affects the nerve and trophic centers, as the toxin of the Klebs-Löffler does in true diphtheria? Is there a pseudo-influenza—the so-called 'grip' of the laity, the ordinary influenzal cold or catarrhal fever—due to a mixed infection, from which the specific germ is absent; comparatively harmless as to the vital centers, and bearing the same relation to influenza vera that pseudodiphtheria does to true diphtheria? If these questions shall be answered in the affirmative by the bacteriologist, as now seems probable, the bacterial diagnosis of influenza, will be only less necessary than

that of diphtheria, and may be followed by as satisfactory results."

The *Medical Age*, editorially commenting upon the same theme, says: "The term grippe seems to have a strange attraction for some people, and every febrile catarrh, of whatever kind, is called 'la grippe.' Gastric cases, headaches, sore throats, coryzas are all grippe. If Pleiffer's bacillus be the actual pathological factor in la grippe, it is to be hoped that some ready method of detecting it may be discovered and that this unfortunate diagnosis may be settled."

I have, in the matter of diagnosis, made a few extracts from a preliminary report on the work done in the laboratory of the Department of Health, of Chicago, along the lines above indicated. These have been furnished me through the courtesy of Dr. Reynolds. The most important feature thus far developed is the feasibility of the bacteriological diagnosis of influenza vera with as much certainty and as much promptness as has been done for diphtheria by the bacteriologists of the Department ever since the Medical Inspector, Dr. Jaques, introduced his direct method of bacterial diagnosis of that disease.

F. E. Wynekoop, First Assistant Bacteriologist for the department, who conducted these investigations, has demonstrated that, after one has become familiar with the appearance of the Canon-Pfeiffer bacillus under the microscope, it may be readily identified in the sputum and mucus of an influenza patient by direct examination without awaiting the process of incubation.

In a disease of such protean manifestations, now simulating typhoid fever, again rheumatic fever, or still again cerebrospinal meningitis or other lesion of the nervous system; a disease that often leaves an impress on its victims for years after, in various forms of mental and nervous disturbance, "from

simple hypochondriasis to melancholia, mania and general paralysis"; a disease that fatally complicates so many other maladies as to increase inordinately the general death-rate of an invalided community—in such a disease, "the demon of influenza," as it has been termed—a prompt and certain diagnosis must, obviously, be of the first importance.

According to Pfeiffer, Canon, Klein[10] and many other observers, the pathogenic organism of influenza is a very minute bacillus which develops in the nasal passages, throat, larynx, bronchial tubes and blood. The organisms are present in great numbers in the bronchial secretions, and are described as occurring only during the acute stages, gradually disappearing as the disease abates. They are said to be constantly present in influenza, and not to be found in any other disorder. These bacilli, we are told, are nonmotile and, so far as is known, do not produce spores. Their length is given as 0.54 micron, and their diameter as 0.24 micron. They are usually solitary, sometimes in pairs or arranged in chains of a few elements. Some observers claim that they are occasionally found in masses, especially in severe cases. They are said to stain poorly, except with certain concentrated, very penetrating stains, and even with these only the ends of the organisms stain well, the middle portion remaining almost unstained.

Kitasato described certain cultural characters by which the bacilli can be readily identified. Their resisting powers are limited. They die quickly, when dried, and are killed within five minutes when exposed to a temperature of 60° C. They will not grow well at a temperature below 26° C., nor above 35° C., when developed on artificial media. Very few materials can be made use of for their cultivation. The best has been found to be bloodserum, which contains a little hemoglobin. Upon this, after a few hours' incubation, "colorless, transparent, drop-like colonies" appear, which resemble "condensed moisture." The colonies have no tendency

to coalesce and, even under the most favorable conditions, soon die, unless frequently transferred.

Such, in substance, is the bacillus of influenza as described by a number of investigators.

In the course of examinations, made in the laboratory of the Department of Health of Chicago, for suspected cases of diphtheria prior to the appearance of influenza in that city, early in December, 1898, a very small bacillus was occasionally found, which, in its morphological characters, corresponded to the organism described by Pfeiffer. With the increase of influenza these organisms were found more frequently, and, in order that more extended observations might be made, physicians were asked to send specimens of the sputum and mucus of their influenza patients to the laboratory, and culture outfits were prepared for this purpose. These were put up in the same manner as those used in the diagnosis of diphtheria, except that the bloodserum contained more hemoglobin.

Human bloodserum was at first used, but, finding that the serum of beef's blood containing hemoglobin answered every purpose, it was finally used altogether, since it was readily procured. Upon this medium cultures were made from the mucous membrane of the tonsils and pharynx and from the bronchial secretions of persons ill with influenza. In many of these cultures, which were comparatively free from other bacteria, transplantations were made to bouillon, a drop of which was immediately transferred to the surface of bloodserum. Three tubes or boxes of serum were usually inoculated from the same drop, and by this means isolated colonies were usually obtained in the second or third tube.

The organism isolated in this manner was found in many cases of clinically typical influenza, and in its morphological, biological and pathogenic characters conformed to the one described in the works on bacteriology. The size and shape were the same and, when examined in the sputum, so also was the

arrangement. Usually the bacilli were found solitary, sometimes in short chains. When a slide was made from a culture, however, they were more often seen in masses. Carbol fuchsin seemed to be the best stain. Other staining solutions were used, but were not satisfactory.

When an examination was made after a culture had been incubated eight or ten hours, the organism stained quite evenly, but after 36 or 48 hours' incubation the characteristic uneven staining was noticed. When bloodserum was used exclusively as a culture medium, growths were obtained that were characteristic and beautiful. The colonies were clear and transparent and, in a measure, resembled minute drops of water or dew.

Influenza and Its Psychoses, Especially Suicidal Mania.

In 1901 there were recorded 7,245 suicide deaths in the United States. In 1899 there were 5,340 such deaths, an increase of 35.6%.

Causes assigned (1901) were as follows:

	No.	Per Cent.
Despondency	2980	41.1
Insanity	647	9.3
Ill health	618	8.5
Domestic infelicity	541	7.4
Liquor	439	6.0
Disappointed love	283	3.9
Business losses	67	0.9
Unassigned causes	1643	22.6

Of the total 7,245 there were 5,850 males and 1,395 females, a proportion of nearly 80% males. Physicians head the list among professional men, the record standing: Physicians, 33%; attorneys, 10%; clergymen, 10%; bankers, 6%; journalists, 6%; college professors, 1%.

The *Medical Record* (March 1, 1902, p. 339) says editorially: "The statistics given above, as to causes, are but roughly drawn up; if close analyses were

made as to motives, the results would be highly instructive from a psychological standpoint. The steady increase of the suicide habit is undoubtedly due, to some extent, to the ease with which poison may be procured." But what causes one to want to procure poison? Is poison any more readily procurable now than a dozen years ago?

In a recent *Weekly Bulletin* (March 1, 1902) of the Health Department of Chicago occurs the following passage: "Against the conditions which have produced these results (an enormous increase of mortality from pneumonia, the chronic diseases, suicide and other forms of violent death—53% more of these latter than a year ago), sanitary effort and administration can do little. Influenza, which has been prevalent, frequently in epidemic form, in all parts of the world during the last dozen years or so, not only disastrously complicates other diseases, but exerts especially a most baneful effect upon the nervous system, causing all forms of mental disturbances, from mere irritability of temper to suicidal melancholia and homicidal mania. The mental equilibrium, not only of individuals, but of nations, has been profoundly affected by this malignant malady during the last decade. The investigations of the coroner's office show that a large proportion of the greatly increased number of suicides in Chicago during this period had previously suffered from the grip. The Department has labored for years to secure proper attention to the importance of the disease, but it is still too often treated indifferently, a trifling ailment that may be 'fought off.'"

A note in the *Medical Record* (June 22, 1901, page 1101) gives the deaths by suicide per 100,000 of population between 1871 and 1900 in five American cities. During the 20 years, 1871-1890, the rate increased from 14.1% to 16.4% in New York, or 16.3%; but in the ten influenza years, 1891-1900, the rate was 21.5—an increase of 52.4% over the previous 20 years' rate. Similarly as to Chicago:

The rate increased from 12.6%, in the first 20 years, to 23.3% in the influenza decade.

Note that, while the total increase between the suicide-rate of the first lustrum, 1871-1875, and the last, 1896-1900, was 66.6% in New York and 82.5% in Chicago, the increase between the first and the fourth lustrums (twenty years) was only 16.3% in New York and 29.3% in Chicago, but was nearly fifty (49.4) per cent. in New York and more than forty-one (41.4) per cent. in Chicago in the ten influenza years, 1891-1900.

Influenza and Its Prevention.

Although the mortality from influenza and its collateral affections, fortunately, fall short of that recorded in the great epidemic, the situation is not free from anxiety. It is probable that, even now, many people fail to realize the fact that influenza is a highly contagious disorder and one of the most virulent of the acute specific diseases. When cholera breaks out in a community every possible precaution is taken to prevent its spread, but in the case of influenza little or nothing is done, and the patient is often unwilling to sacrifice his social engagements. It is the reckless exposure of the infected which makes the disease so difficult to eradicate. Every one is exposed, more or less, to the danger of being invaded by the bacillus, and it is difficult to devise prophylactic measures on which absolute reliance can be placed. Much, however, may be done by attention to a few simple rules.

When a person is ill with influenza, it is better not to visit him or, if a visit is imperative, it is advisable to avoid unnecessary personal contact. After the interview the hands should be thoroughly washed in an antiseptic solution and the outer garments should be aired by being exposed to a cur-

rent of fresh air or, better still, to the direct rays of the sun. The condition of the general health of those exposed to infection should be maintained by plenty of outdoor exercise, by good food and the avoidance of indulgence in alcohol. At the onset of the initial symptoms the patient should remain in bed and should at once obtain medical advice. No reliance should be placed on popular remedies, for the complications are so grave that the best-possible treatment is required. All articles, such as sheets and pocket handkerchiefs, which have been used in the sickroom, should be put into a vessel containing an efficient disinfectant. That recommended by many sanitarians is made by mixing half an ounce of corrosive sublimate, one fluid ounce of hydrochloric acid and 5 gm. of commercial aniline blue in 3 gallons (a bucketful) of water. It is, of course, poisonous and a good disinfectant; besides, it is cheap. Articles, after being allowed to stand for some time in this mixture, should be rinsed in clear water for three or four hours before being sent to the wash. Clothing may be disinfected in a suitable disinfecting apparatus by heat, and local sanitary authorities should be urged to give notice of their willingness to undertake this duty. After the patient has vacated his room, the furniture should be removed and cleansed and the room disinfected, preferably with formalin. These may seem unnecessary precautions, but the disease is so infectious, and its consequences so far-reaching, that it is wise to treat its risk seriously.[11]

1. H. Fehr. Influenza som Aarsag til Sindssygdom. Copenhagen, 1889. See Journal Mental Science, July, 1899.
2. British Medical Journal, 1899, Feb. 18, p, 429.
3. American Medicine, April 20, 1901, p. 104.
4. April 1, 1899, p. 409.
5. Mental Diseases, New York, 1897, p. 361.
6. Diseases Nervous System, Philadelphia, 1900, Vol. II, p 900.

7. Mental Diseases. Berkeley, New York, 19000, p. 358.
8. Extract from a review in the Journal of Mental Science, July, 1899, of H. Fehr's work on Influenza.
9. F. W. Reilly, Assistant Commissioner of Health, Chicago.
10. Dr. Wynekoop's Preliminary Report.
11. British Medical Journal, March 4, 1899, p. 550.